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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,026	10/02/2006	Frans-Josef Meyer-Almes	BHC 03 1002	5952

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EXAMINER	
TURK, NEIL N	

ART UNIT	PAPER NUMBER
1797	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/575,026	MEYER-ALMES ET AL.	
	Examiner	Art Unit	
	NEIL TURK	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-16 and 18-29* is/are pending in the application.

4a) Of the above claim(s) *20-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-16,18 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/20/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Remarks

This Office Action fully acknowledges Applicant's remarks filed on April 20th, 2010. Claims 10-16 and 18-29 are pending. Claims 20-29 have been withdrawn from consideration. Claims 1-9 and 17 have been cancelled.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 20th, 2010 has been entered.

Specification

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: The specification lacks antecedent basis for the claim terminology "modifying agent".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-16, 18, and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a molecule being a peptide or peptidomimetic and modification in the form of phosphorylation or dephosphorylation, elimination, or addition, does not reasonably provide enablement for the particular modifications listed in claim 10. The specifiation is not enabled for the modification to the molecule being sulfation/desulfation, methylation/demethylation, oxidation/reduction, acetylation/deacetylation, amidation/deamidation, cyclization/decyclization, a conformational change, a cleavage or addition of an amino acid residue or peptide, coupling of amino acids or peptides to the molecule, ring expansion or ring contraction, rearrangement, or substitution. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims. Applicant's disclosure does not provide enabling support for the above-noted modifications to the molecule. Applicant's disclosure in paragraph [0034] mentions such modifications, but the discussion of the modification is presented only in a theoretical and prophetic sense.

This likewise applies to the limitations of **claim 18**, in which there is not an adequate disclosure with respect to sulfation, methylation, oxidization (assumed intended as oxidation), acetylation, amidation or cyclization of the molecule, and Applicant's disclosure is limited to phosphorylation of the molecule.

An analysis of the Wands Factors (In re Wands, *858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1998)* further substantiates why the specification is not enabling.

1. The nature of the invention

The nature of the invention is indicating a modification to a molecule by way of measuring the difference in fluorescence lifetime between a fluorescently labeled molecule and a fluorescently labeled molecule to which a modifying agent has been applied.

2. The state of the prior art

The state of the prior art is said to be related to fluorescence polarization in measuring phosphorlyation/dephosphorylation in proteins (see paragraphs [0019-0028] of Applicant's pre-grant publication US 2007/0042500). This is likewise seen in the prior art of Burke (US 2001/0004522) who discloses a method for detecting phosphorylated amino acids by using a comparision fluorescence polarization measurements. Additionally, the prior art of Pollok et al. (US 6,410,255) who discloses the use of optical probes useful for an optical sensor of post translational type modifications, such as phosphorylation. Additionally, the prior art of Doering (US 2004/0259183) provides methodology to measuring the presence or absence of chemical groups, such as phosphate groups, attached to biological molecules by measuring a difference in fluorescence lifetime.

3. The level of one of ordinary skill in the art

The level of one of ordinary skill in the art is drawn to a person of ordinary skill in the fields of optics, chemistry, and biochemistry.

4. The predictability of lack thereof in the art

The art has a high degree of unpredictability as this art is previously unsubstantiated and unknown. Applicant's specification does not remedy such a high degree of unpredictability, as the specification does not substantiate the newly-founded art by explaining in-depth the scientific principles involved and providing probative evidence of its actual practice and application.

5. The amount of direction or guidance present

The specification provides no direction or guidance that teaches how to make or use the invention, as claimed. The specification provides only generic guidance that the method has potential to be applicable to the above-noted modifications. The specification does not, however, provide direction or disclosure which shows that changes in FLT would necessarily result and provide connecting evidence of the listed modifications. The specification does not make clear how the addition or removal of such groups from a molecule would provide to yield such a detectable modification through FLT measurement. Further, modifications such as conformational changes, rearrangements, and ring expansion/ring contraction provide modifications which are

fundamentally different from the disclosed methodology involving phosphorylation/dephosphorylation which involve addition or removal of a group that is not akin to the above modifications (conformational changes, ring expansion/contraction, and rearrangements).

6. The presence of absence of working examples

The specification does not provide any working examples. Whereas the specification provides examples of the differences in fluorescence lifetime of a phosphorlyated and non-phosphorylated peptide (see paragraphs [0044-0062], for example, in Applicant's pre-grant publication US 2007/0042500).

7. The breadth of the claims

The breadth of the claims encompass a method in which encompasses any possible modification to any type of molecule. This is seen as claim 10 generically recites a molecule and recites the above-noted modifications, as well as denoting modifications of substitution, elimination, or addition to the molecule. The breadth of the claims is not commensurate with Applicant's disclosure. Applicant's disclosure discusses that the molecule may be organic or inorganic (thereby, any molecule), but the discussion in the disclosure is limited to that of peptides and peptidomimetrics (in the class of biopolymers, proteins), and lacks description with respect to other molecules and does not provide disclosure of the methodology with respect to inorganic molecules in either of a generic or specific example thereof. Applicant's disclosure is

limited to peptides or peptidomimetrics and the modification of phosphorylation/dephosphorylation (thereby, also addition or elimination to the molecule).

8. The quantity of experimentation needed

An undue amount of experimentation would be needed to practice the invention. This is seen because Applicant's disclosure does not define how to make/use the invention for the methodology in which the theorized modifications could be indicated. Further, the choice of the molecule is unbounded and the disclosure lacks even a description on the utilization of inorganic molecules in general. Further, Applicant does not provide working examples and data, and show how one may make or use the invention as claimed. Further, Applicant's claims are drawn to any sort of modification being possible by way of the inventive method. Herein, in combination with the inadequate disclosure, there would be undue experimentation necessary for the vast amount of molecules, modifications and mechanisms involved therein in order to substantiate such purported capabilities.

Claim 14 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the molecule being a peptide or peptidomimetric, does not reasonably provide enablement for the modifying agent being a peptide or peptidomimetric. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention

commensurate in scope with these claims. Applicant's specification (by way of pre-grant publication US 2007/0042500) in paragraphs [0033,0034,0039] describes that a peptide or peptidomimetric may be molecules of the claimed method, and are not modifying agents.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 10-16, 18, and 19 are rejected under 35 U.S.C. 102(e) as being anticipated by Doering (US 2004/0259183).

Doering discloses a method for measuring the presence or absence of chemical groups, in particular phosphate groups, attached to biological molecules in a sample in which the molecules are tagged with fluorescent markers and the fluorescent markers are activated by means of irradiating the sample with light. Doering discloses that the method is characterized by a) the use of a fluorescent marker, the fluorescence lifetime of which assumes a different value depending upon the presence or absence of phosphate groups attached to the biomolecule; b) measurement of the fluorescence lifetime of the fluorescent marker attached to a biomolecule and selected in accordance

with step a); and c) classification of the biomolecules in accordance with the presence or absence of phosphate groups attached to these based on the different fluorescent lifetime of each (abstract; pars. [0037-0044]). Examiner asserts that in measuring the fluorescence lifetime to reflect the state of the peptide, the phosphorylation or dephosphorylation thereof reflects a modification of an addition (phosphorylation) or elimination (dephosphorylation) to the biological molecule. Doering discloses that fluorescein is a suitable fluorescent marker (par. [0011]). Examiner asserts that use of such dyes as labels to the biological molecule utilize a covalent bond therebetween, and further, the molecules which make up the covalent bond are said to comprise a spacer. Doering further discloses that an enzyme, such as a kinase, may be utilized as the modifying agent (par. 0017]). Doering additionally discloses that the molecule may be a protein or peptide (pars. [0027-0031]). With regard to claim 18, Doering discloses that enzymes such as oxidoreductases catalyze redox reactions, with oxidation resulting in the loss of electrons and a reduction in the acquisition of electrons. Doering discloses that it is possible that the modification of a fluorescence lifetime signal can be observed for a fluorescent marker which is located in the direct vicinity of an active oxidoreductase site, indicating the migration of electrons through various amino acid side chains within the enzyme or substrate during the catalytic transition (difference in property as a state of oxidation). With regard to claim 19, the limitations are drawn to intended use of the method, in which intended use of the method is not afforded patentable weight. As Doering discloses the method of claim 10, Doering is said to be capable of such an intended use.

Response to Arguments

Applicant's arguments with respect to claims 10-16, 18, and 19 have been considered but are moot in view of the new ground(s) of rejection, as discussed above. Further, an objection to the specification has been added, as discussed above.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NEIL TURK whose telephone number is (571)272-8914. The examiner can normally be reached on M-F, 9-630.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on 571-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

NT /Jill Warden/
Supervisory Patent Examiner, Art Unit 1797